

Preterm Labor: Disruption of a Reproductive Agreement

Lucio Zichella

1st Chair of Obstetrics and Gynecology, Policlinico Umberto I, University of Rome “La Sapienza”, Rome, Italy

Abstract

Modern biology shows that all functions depend on the integration among different organic systems and environment. In considering the pathophysiology of preterm labor, I like to remember how this situation is the result of differently operating factors, which are not easily defined. We must consider two main conditions: a primitive, “sine causa” preterm delivery, and the situations in which fetal or maternal abnormalities are present, as a cause of preterm labor.

Although many risk factors have been defined and many programmes of primary and secondary prevention have been established, the incidence of preterm labor did not decrease in our society, but, on the contrary, showed a little increase in the last years.

It is so evident that, beyond different organic conditions, new psychological and social factors, which are not easily controlled, interfere negatively, in maintaining the high incidence of preterm delivery. We think that the psychobiological relationships between the mother and the fetus-newborn can be considered as a “Biological Agreement” in which both part have a fundamental role. It is then evident that a correct maintenance of the Reproductive Agreement is based on fine homeostatic mechanisms which can be variably deregulated by fetal influences and/or different socio-environmental situations. As a consequence of considering preterm labor as the result of a disadaptation of the psychobiological linkage between the mother and the fetus/placental unit, an intensive follow-up of the preterm baby becomes mandatory: the earliest, post-partum contacts of the mother with her baby are certainly able to compensate a precedent disequilibrium.

Correspondence to: Prof. Lucio Zichella, M.D., 1st Chair of Obstetrics and Gynecology, Policlinico Umberto I, Viale del Policlinico 155, 00161 Rome, Italy
Mail private address: Prof. Lucio Zichella, Via C. Linneo 3, 00197 Rome, Italy

Zusammenfassung

Die moderne Biologie zeigt, daß alle Lebensfunktionen auf der Integration verschiedener organischer Systeme und der Umgebung beruhen. Bei der Betrachtung der Pathophysiologie vorzeitiger Wehen möchte ich vergegenwärtigen, daß diese Situation das Ergebnis verschiedener wirksamer Faktoren ist, die nicht leicht definiert werden können. Wir haben zwei Grundsituationen: eine ursprüngliche, vorzeitige Entbindung ohne eigentliche Ursache und die Situation, in der fötale oder mütterliche Regelwidrigkeiten als Ursache der vorzeitigen Wehentätigkeit bestehen.

Obwohl viele Risikofaktoren erkannt wurden und viele Programme primärer oder sekundärer Prävention eingerichtet wurden, ging die Häufigkeit vorzeitiger Wehentätigkeit in unserer Gesellschaft nicht zurück, sondern zeigte im Gegenteil in den letzten Jahren einen geringen Anstieg.

Es ist offensichtlich, daß ausser organischen Ursachen neue psychologische und soziale Faktoren, die nicht leicht auszuschließen sind, dazu beitragen, daß die Häufigkeit der vorzeitigen Wehentätigkeit hoch bleibt. Wir stellen uns vor, daß man die psychologische Beziehung zwischen der Mutter und dem Fötus als ein "Biological Agreement" ansehen kann, dessen Aufrechterhaltung von beiden Partnern abhängig ist. Dann ist offensichtlich, daß die Aufrechterhaltung der reproduktiven Agreements auf subtilen homeostatischen Mechanismen beruht, die durch fötale Einflüsse gestört werden können und/oder durch verschiedene soziale und situative Einflüsse. Als Konsequenz der Betrachtung der vorzeitigen Wehentätigkeit auf das Ergebnis eines Anpassungsverlustes in der psychologischen Verbindung zwischen der Mutter und der föto-plazentaren Einheit ergibt sich die Forderung nach intensiver Begleitung und Beobachtung des frühgeborenen Kindes: Die ersten nachgeburtlichen Kontakte der Mutter mit ihrem Kind können sicherlich ein vorangegangenes Ungleichgewicht ausgleichen.

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Modern biology shows that all functions depend on the integration among different organic systems and environment. Recent advances of molecular biology showed a constant equilibrium among cells, body and environment, broadening the concept of "Homeostasis", first proposed by the American physiologist W. Cannon.

The presence of an equilibrium among different compartments can be evidenced in numerous psychobiological functions: in the human infant reproductive function although largely autonomous, is under a strict control of a complex homeostatic system composed by the environment, the mother and the fetus. So

far reproduction cannot be confined in a simple mechanistic dimension, which is the only one considered, still today, by many authors.

In considering the pathophysiology of preterm labor, I like to remember how this situation is the result of differently operating factors, which are not easily defined. Moreover, these same factors are often different in the human and in the animals: as a result, all the studies conducted in experimental animals are not directly comparable to the human^{6,7}.

Further distinction between human and animals is created by the difference existing at the level of the fetal placental unit which is the complex of biochemical pathways necessary to the maintenance of pregnancy and in some way in the induction of labor^{3,5}. The mother and the fetus both participate actively to the constitution of fetal placental unit. In the humans and primates placenta lack 17OHase: direct synthesis of estrogen from progesterone is consequently impossible. Maternal cholesterol is then utilized for progesterone synthesis as well as fetal and maternal androgens (Dhas) are used for estrogen production. In other mammals placental 17OHase lets the fetal placental unit utilize progesterone as a source for estrogen biosynthesis⁶. The fetus is then able, through the induction of cortisol-primed aromatase activity, to set the exact timing of delivery, through a reduction of the progesterone/estrogen ratio^{8,9,10,19,20}.

In conclusion, in the human, the fetus cannot induce those metabolic changes, that induce the onset of delivery, which can be, on the contrary, described in other species like the sheep. As it concerns preterm labor we must consider two main conditions: a primitive, "sine causa" preterm delivery, and the situations in which fetal or maternal abnormalities are present, as a cause of preterm labor^{16,17}. It is not possible to hypothesize the *primum movens* of the onset of labor in primitive conditions². In the human labor is an automatic event but it can be influenced by different optionalities which are derived from the phylogenesis and can become operative, for example, in response to biological or psychosocial distress, favouring preterm labor.

The complexity of the factors involved explains all the difficulties found in understanding the pathogenesis and in setting on an effective prevention of preterm labor^{4,22}.

The risk factors for preterm labor were first studied by Pinard²¹. This author correlated the incidence of pre-term labor with discomfortable socio-economic conditions: women who worked in the Vangirard laundries had a higher incidence of pre-term labor, with respect to the controls, unless they could have an adequate relax during the last weeks of pregnancy. A second important report by Debré²³ in 1934 examined medical and social causes of perinatal mortality, pre-term labor was peculiar of young multiparous women from the low social classes, who had a stressful activity. This latter condition was recognized to be preminent. Moreover, Debré pointed out the importance of perinatal care.

Some nosographic problems emerge in the definition of preterm: the lack on an exact estimation of the length of pregnancy in pre-ecographic era, limit the value of these earlier reports. Many authors, in the past, examined neonatal weight and defined as premature any infant weighting less than 2500 g. In this way, true prematures, small for gestational age and constitutionally small new-

borns were often confused. The risk factors pointed out by these studies must then be critically reconsidered, for the purpose of an effective prevention.

Recent reports on preterm labor devided the risk factors in:

Demographic factors

- Maternal age (< 17 years or > 35 years)
- Low socioeconomic standing
- Maternal education
- Race

Behavioural factors

- Smoke
- Nutrition
- Stressful activity
- Inadequate prenatal care

Medical or obstetric pregravidic factors

- Two or more previous preterm births
- Uterine anomaly
- Two or more second-trimester abortions
- Incompetent cervix
- Urinary tract infections
- Large uterine myoma
- Genetic?

Medical or obstetric gravidic factors

- Twin gestation
- Polidramnios
- Vaginal infections
- Cervical dilatation without labor (> 1 cm)
- Vaginal bleeding after the 12th week
- Uterine irritability

Although many risk factors have been defined and many programmes of primary and secondary prevention have been established¹⁵, the incidence of preterm labor did not decrease in our society, but, on the contrary, showed a little increase in the last years. In the U.S. the incidence was 8.4% of all labors in 1980 and 10.1% in 1986¹⁶. In Germany and France it is of 8% and 9% respectively. It is so evident that, beyond differnt organic conditions, new psychological and social factors, which are not easily controlled, interfere negatively, in maintaining the high incidence of preterm delivery^{11,12,27,28,30,35}. We think that the psychobiological relationships between the mother and the fetus-newborn can be considered as a "Biological Agreement" in which both parts have a fundamental role. The end of the first part of this agreement (delivery) has a precise timing: it offers, however, different optional alternatives which come from phylogenesis. For example, the fetus can activate, in some dangerous conditions a series of mechanisms of defense which let him survive in the intrauterine environment, however, as a last attempt of escaping from a very hostile environment, he can trigger the onset of preterm labor. In this way the fetus can no more be consid-

ered also in the human as a passive guest, growing in the uterus, but becomes a fundamental part of a complex, integrated system. It is then evident that a correct maintenance of the Reproductive Agreement is based on fine homeostatic mechanisms which can be variably deregulated by different socio-environmental situations. According to McLeans, the contemporaneous presence of two drives "Self preservation" and "Preservation of species" plays a fundamental role in our opinion also in the mother-fetus interaction which is the base of the "Reproductive Agreement". A positive balance between these two drives, conditioned by emotional, cultural, anthropological influences is essential for a positive outcome of reproduction, maintenance of pregnancy, breast feeding and fetal maternal bonding^{1,2,13,24,29}.

Probably considering the complexity of the psychodynamic mechanisms, the problems are not so simple: the final outcome should be the result of the algebraic addition of the different positive and negative factors affecting these two drives.

Different clinical situations from abortion to preterm labor and modifications of maternal attachment can then be considered as a disadaptation between the mother and the fetus, due to individual or external determinants.

As a consequence of considering preterm labor as the result of a disadaptation of the psychobiological linkage between the mother and the fetus, an intensive follow-up of the preterm baby becomes mandatory: the earliest, post-partum contacts of the mother with her baby are certainly able to compensate a precedent disequilibrium. The standards of assistance, during labor and post-partum, towards a preterm infant are still not well identified. It is, however, well documented the importance of the first mother-newborn interaction. Recent studies evidenced a high incidence of abuse and walking problems among babies who underwent preterm labor^{24,25,26}. The long period of separation in the post-partum does not allow, especially in the case of the preterm newborns, a correct establishment of the mother-infant bonding¹⁴. The psychobiological attitudes of the mother are then of the greatest importance in determining a correct linkage with her baby. Many authors point out that mothers with a good psychological equilibrium and an adequate social background better accept the prematurity of their baby; it is true, however, that all the mothers show some behavioural changes even before a definitive diagnosis of prematurity. It is a sensation of "abnormality" the one that the mother perceives very soon; as a consequence she pays a great attention towards the baby (touching, speaking and smiling to him continuously). Between 6 and 12 months after birth a relative separation of the mother from the baby occurs: only after the first year is the mother completely aware of the short height and low weight of her infant^{26,29}. It is difficult to determine which behaviours of the preterm babies are able to attract mother's intention; the two psychobiological systems, maternal and fetal and/or neonatal, are strictly linked by programmed "channels of communication": breast feeding reflects, at least in part, a functional integrity of CNS of the baby, and represents a preferential way of interaction of the newborn with his mother. In this way, positive attitudes towards maternal attachment and breast feeding are important by integrating and improving situations existing during pregnancy to guarantee an

adequate second part of the "Reproductive Agreement" between mother and newborn. So far, not only the biological aspects, also the psychobehavioural and sociocultural implications of pregnancy and labor need to be elucidated for an effective prevention in different clinical situations such as premature labor through the establishment of an ideal psychobiological correlation among mother, fetus and neonate. We feel that a stressful situation is at the basis of preterm labor also for those women who are not classical "candidates" lacking of psychological or cultural discomfort. In these cases an exasperate wish of becoming "mother" can lead to the induction of preterm labor^{31,32,33}.

It is so extremely important to evaluate all the variables such as the biological, sociological and psychodynamic determinants involved in so defined preterm labor sine causa; only a decodification of these factors will assure an adequate prevention to those pregnancies at risk for preterm labor.

References

1. Newton, R. W. (1984). Psychological stress in pregnancy and its relation to low birth weight. *Br. Med. J.* **288**, 1191-1194
2. Morrison, J. C. (1990). Preterm birth: a puzzle worth solving. *Ob. and Gynecol.* **76** (suppl.), 5s-12s
3. Casey, M. L. (1988). Biomolecular processes in the initiation of parturition: decidual activation. *Clin. Obst. Gynecol.* **31**, 533-552
4. Herron, M. (1982). Evaluation of a preterm birth prevention program: preliminary report. *Ob. and Gynecol.* **59**, 452-456
5. Scott, W. (1989). 5-hydroxyeicosatetraenoic acid, leukotriene C4 and prostaglandin F2alfa in amniotic fluid before and during term and preterm labor. *Am. J. Obstet. and Gynecol.* **161** (5), 1352-1359
6. Liggins, C. G. (1977). Control of parturition in man. *Biol. Reprod.* **16**, 39-56
7. Liggins, C. G. (1973). The mechanism of initiation of parturition in the ewe. *Recent Prog. Horm. Res.* **29**, 111-159
8. Romero, R. (1987). Arachidonate lipoxygenase metabolites in amniotic fluid of women with intraamniotic infection and preterm labor. *Am. J. Obstet. Gynecol.* **157**, 1454-1460
9. Szekeres-Bartho, J. (1986). Immunologic factors contributing to the initiation of labor - lymphocyte reactivity in term labor and threatened preterm delivery. *Am. J. Obstet. Gynecol.* **155**, 108-112
10. Hercz, P. (1990). Serum dehydroepiandrosterone and cortisol concentration in the maternal-fetoplacental hormonal system in elective caesarean section and spontaneous vaginal delivery in the 28th to 36th and 40th weeks of pregnancy. *Gynecol. Obstet. Invest.* **29**, 112-114
11. Morrison, J. C. (1990). Cost/health effectiveness of home uterine activity monitoring in a medicaid population. *Ob. and Gynecol.* **76**, 76s-81s
12. Creasy, R. (1990). Prevention of preterm birth: clinical opinion. *Ob. and Gynecol.* **76**, 2s-4s
13. Zuckerman, B. (1989). Depressive symptoms during pregnancy: relationship to poor health behaviors. *Am. J. Obstet. Gynecol.* **160**, 1107-1111
14. Eisenberg, L. (1981). Social context of child development. *Pediatrics* **68**, 705-712
15. Iams, J. (1990). Symptoms that precede preterm labor and premature rupture of the membranes. *Am. J. Obstet. Gynecol.* **162**, 486-490
16. Morrison, J. C. (1990). The incidence of preterm labor and specific risk factors. *Ob. and Gynecol.* **76**, 85s-89s

17. Fedrick, J. (1976). Factors associated with spontaneous preterm birth. *Br. J. Ob. Gynecol.* **83**, 342–350
18. McAnarney, E. R. (1990). Maternal psychological stress/depression and low birth weight. *AJDC* **144**, 789–791
19. Procianoy, R. S. (1983). Umbilical cord cortisol and prolactin levels in preterm infants. *Acta Ped. Scand.* **72**, 713–716
20. Bernal, L. A. (1987). Corticosteroid levels in human fetal blood at midgestation and at term. *J. Ob. Gynecol.* **156**, 112–113
21. Pinard, A. (1895). Note pour servir à l'histoire de la puériculture. *Bull. Soc. Med. Hyg. Prof.* **XVIII**, 326
22. Papiernik, E. (1973). A prospective study of the prevention of prematurity and dysmaturity. *Perinat. Med.* **4**, 325
23. Debré, R. J. (1934). Enquete internationale sur la mortalité foeto-infantile. *Rev. Hygiene* **1**, 6
24. Reisch, S. K. (1984). Promoting awareness: the mother and her baby. *Nurs. Res.* **33** (5), 271
27. Newton, R. W. (1979). Psychosocial stress in pregnancy and its relation to the onset of premature labor. *Br. Med. J.* **2**, 411–413
28. Mamelle, N. (1984). Prematurity and occupational activity during pregnancy. *Am. J. Epidemiol.* **119**, 309
29. Brooke, O. G. (1989). Effects on birth weight of smoking, alcohol, caffeine, socio-economic factors and psychosocial stress. *Br. Med. J.* **289**, 795
30. Papiernik, E. (1989). Psychological and social aspect of pre and perinatal care. *J. Psych. Obst. Gynecol.* **10** (s. 1), 3
31. Kragt, H. (1989). Psychosocial health and threatened preterm birth. *J. Psych. Obst. Gynecol.* **10** (s. 1), 105
32. Budd, K. W. (1989). Self-coherence: a psychosocial predictor of preterm delivery. *J. Psych. Obst. Gynecol.* **10** (s. 1), 104
33. Mamelle, N. (1989). Psychological attitudes during pregnancy and preterm birth – a prospective study. *J. Psych. Obst. Gynecol.* **10** (s. 1), 51